

# Infectious Hepatitis— Presumedly Food-borne Outbreak

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IT is commonly believed that the hepatitis seen in epidemic proportions in members of the Armed Forces in 1942–1943 was a human infectious disease acquired from human serum used in preparation of the yellow fever vaccine then in use.<sup>1</sup> This belief presupposes that there naturally occurs in man a hepatitis due to a virus which may under certain conditions be present in the serum or plasma. If analogy with other virus diseases is valid, it may be presumed that a group of agents might cause a disease having similar clinical characteristics.<sup>2</sup> It would seem worth while, therefore, to record each outbreak of what clinically appears to be infectious hepatitis in which the mode of transmission seems reasonably clear even though conclusive evidence as to the viral cause or exact mode of transmission may not be available.

In the late spring of 1944 an outbreak of infectious hepatitis occurred among students at Western Reserve University School of Medicine. The outbreak was explosive, onset dates for all 24 cases falling between May 26 and June 5 (Table 1).

Cases developed in all four classes: 9 in the first year, 7 in each of the second and third years, but only 1 in the fourth year. All patients were members of a single fraternity.

TABLE 1

*Day of Onset of Symptoms in 24 Cases*

<i>Date</i>	<i>Number of Cases</i>
May 26.....	1
27.....	2
28.....	3
29.....	0
30.....	3
31.....	3
June 1.....	4
2.....	4
3.....	1
4.....	2
5.....	1

Early in April, two first year students were hospitalized because of jaundice. These two men were not members of the fraternity and, as far as could be determined, had had only casual contact with the subsequent patients. One case developed in a dental student two months after the principal outbreak, but again history of only very casual contact was obtained. Other than these, no cases were recognized during the year of 1944.

Data relative to the eating habits of members of the fraternity are shown in Table 2. Of 101 members of the fraternity, only 14 men lived in the house and ate all of their meals in the house dining room. Four cases developed in this group, an attack rate of 28.5 per cent. Sixty men regularly ate all or part of their meals at the house but

did not live there. Among these there were 20 cases, an attack rate of 33.3 per cent. The remaining 27 members either ate no meals or only an occasional one at the house. No cases occurred in this group. No cases occurred in students other than members of the fraternity, in spite of close daily contact in classroom and laboratory. These facts would indicate that regular eating at the fraternity dining room was an important factor in determining the risk of attack.

TABLE 2

*Relationship of Meals Eaten at Fraternity House to Attack Rate*

<i>Frequency of Eating at Fraternity House</i>	<i>Total</i>	<i>Patients</i>	<i>Attack Rate Per cent</i>
Eating regularly			
Resident	14	4	28.5
Non-resident	60	20	33.3
Eating infrequently	20	0	0.0
No meals *	7	0	0.0
All members	101	24	23.8

\* March 1 to June 1, 1944.

An analysis of the number of meals eaten at the house revealed both more regular and more frequent eating by the patients than by the nonpatients. Since an incubation period of from 20 to 34 days<sup>3</sup> has been reported in experimentally produced infectious hepatitis, a study was made of meals eaten between April 10 and May 15. This showed that the patients on the average ate 47.5 meals out of a possible 84 served, as compared with 25.9 for nonpatients, a ratio of 1.8 to 1. For a period of 3 months prior to the outbreak the ratio for meals eaten by patients to those eaten by nonpatients was the same.

An attempt to select a single day on which the infection might have occurred was disappointing. On no day did all the patients eat all their meals at the house. Considering only lunch and dinner, since the proportion of breakfasts eaten by both patients and non-

patients was relatively small, there were two days, March 8 and 9, on which every patient ate either lunch or dinner or both. On those days, respectively, 28 and 31 of the 77 nonpatients ate neither lunch nor dinner at the house. Infection occurring on these dates seems unlikely in view of the experimental work reported, as an incubation period of 80 days would be much too long.

There were, however, periods of two successive days each on which every patient ate either lunch, dinner, or both on one or the other or both days. These periods were April 27 and 28 and May 9 and 10. On the first of these two periods, the number of nonpatients who ate neither lunch nor dinner was 18, on the latter 31. Thus either of these two periods might have been the days on which infection occurred.

Investigation showed that the kitchen and dining rooms were clean. Left-over food was stored in refrigerators. Pasteurized milk was obtained daily in 2 gallon jugs and kept covered, but not on ice, until serving. All water used came from the regular municipal supply. Inspection showed no evidence of rat infestation.

Unfortunately no record was kept of the food served at individual meals. Consequently no single article of food could be incriminated. A study of the eating habits of the patients and a sample of nonpatients revealed no essential difference. There had been no symptoms of unusual illness on the part of any employees handling food. Nevertheless, evidence points strongly to an epidemic spread through some article or articles of food served in the fraternity dining room.

The clinical picture of the disease was quite uniform in the great majority of the cases. A number of the salient features of the disease are presented in Table 3. In most cases the onset of the disease was insidious. Malaise and general myalgia gradually increased,

TABLE 3  
*Frequency of Various Clinical Signs in 24 Patients*

<i>Clinical Signs</i>	<i>Number in Which Sign Occurred</i>	<i>Remarks</i>
Hyperemia of pharynx	11	Slight to moderate degree. No associated symptoms.
Superficial lymphadenopathy	6	Usually cervical chain only. Generalized in 2.
Enlarged spleen	6	In one case extended 4 cm. below costal margin. Persisted for 4 to 14 days.
Enlarged liver	20	Varied from a barely detectable enlargement to one extending 4 cm. below costal margin. The liver was fairly firm, edge smooth and somewhat rounded. Usually somewhat tender. Persisted for 4 to 14 days.
Bradycardia	22	Lowest pulse rates were 44 to 60.
Leukopenia	16	Below 5,000 WBC's per cu. mm. Highest count, 6,350.
Clay colored stools	10	
Albuminuria	12	Slight to moderate.

chilly sensations were noted, and fever appeared which might rise to 38° or 39° C. About half of the men complained of orbital pain at the time of onset. Anorexia appeared early and by the end of 4–7 days had become severe. By this time nausea was present also, and in many cases was associated with almost intractable vomiting. Dark urine was noticed soon after the onset of illness. In a few cases, it was almost the first sign of disease. By the 4th or 5th day the fever had begun to subside, and within a day or two jaundice was evident and this continued to deepen for several days.

By the end of the second week definite improvement was evident in nearly all cases. Appetite returned, epigastric distress subsided, and sometimes a decrease in the depth of jaundice was apparent. Asthenia persisted in most cases for some weeks after the disappearance of all other symptoms or signs of the infection.

Certain features of the illness which these men presented were strongly suggestive of mononucleosis. Although there were no complaints referable to the pharynx, a hyperemia of definitely

abnormal degree was present in half of the patients, and superficial lymphadenopathy was present in one-fourth. Usually this involved only the cervical chain of lymph nodes. In 6 cases the spleen was palpable, in one case extending 4 cm. below the costal margin. In contrast to mononucleosis, the total white blood count was low, a decrease involving chiefly the neutrophilic cells, but usually with a disproportionate increase in cells classed as monocytes, the percentages of which ranged from 7 to 26. The liver was palpable in almost all cases and usually was tender. The icterus index was high in all cases, the highest being 72. The cephalin flocculation test was positive in all cases at some time during the illness. The prothrombin content of the blood was abnormally low in several cases, but no tendency to hemorrhage was observed. Electrocardiograms were made in a number of cases, the findings of which are being reported elsewhere.<sup>4</sup> Essentially, there was a depression of the amplitude of the T wave, the extent of which bore no relation to the depth of the jaundice.

During the period of the outbreak

7 other members of the fraternity, 5 of whom ate regularly at the house, exhibited symptoms possibly caused by hepatitis. In none was jaundice observed.

#### COMMENTS

The clinical picture of the disease in these patients was similar in all particulars to that which occurred among military personnel, and to spontaneous outbreaks in civilian populations.

The possibility of spirochetal jaundice was excluded by studies made by Dr. E. E. Ecker. Blood plasma was examined directly in the darkfield for leptospira. Blood and urine was seeded into Schüffner's leptospira medium and inoculated into young (less than 250 gram) guinea pigs. The urine was alkalized before collection for culture and animal inoculation. The sera of several patients were examined in convalescence for the presence of leptospiral agglutinins. All of these examinations were negative.

A notable feature of the principal outbreak was its explosive character, suggesting a limited period of exposure of a large group of men. No relation could be discovered between the outbreak and two previous cases of jaundice occurring in members of the student body, and no secondary cases were recognized in spite of the close classroom association of men early in the disease with presumably susceptible individuals. In the case of the dental student, the contact was at second hand. Evidence points clearly to the fact that this infection was confined to one fraternity and those who ate regularly at this fraternity had a much higher attack rate than did other members. The evidence of marked disturbance of the lymphatic system was unusually great.

No characteristic change in the differential distribution of white cells could be established and no cells having the characteristics of the abnormal ones which appear in infectious mononucleosis were recognized, but a total of 9 (37 per cent) of the patients had lymphadenopathy, either cervical, general superficial, or splenic, and a white blood count which bore some resemblance to that of mononucleosis.

#### SUMMARY

An outbreak of infectious hepatitis among medical students is described. The outbreak was explosive, involved only members of one fraternity, and primarily those who ate regularly at the fraternity dining table. The cases were not traceable to previous cases, and so far as could be determined led to no secondary cases.

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